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EXAMINER

KAM, CHIH MIN

ART UNIT PAPER NUMBER

1656

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/485,571

Applicant(s)

CALAS ET AL.

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-20,24,29 and 30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20,24 and 29 is/are rejected.
- 7) ☒ Claim(s) 18,19 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 18-20, 24, 29 and 30 are pending.

Applicants' amendment filed January 3, 2006 is acknowledged, and applicants' response has been fully considered. Claims 18, 20, 24, 29 and 30 have been amended, and claim 33, 34, 37 and 38 have been cancelled. Thus, claims 18-20, 24, 29 and 30 are examined.

Withdrawn Claim Objection

2. The previous objection to claims 20 and 37, is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at page 6 of the amendment filed January 3, 2006.

Withdrawn Claim Rejections - 35 USC § 112

3. The previous rejection of claims 18, 19, 29, 30, 33, 34, 37 and 38 under 35 U.S.C.112, first paragraph, scope rejection, is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 6-7 of the amendment filed January 3, 2006.
4. The previous rejection of claims 18-20, 24, 29, 30, 33, 34, 37 and 38 under 35 U.S.C.112, first paragraph, written description, is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 6-7 of the amendment filed January 3, 2006.
5. The previous rejection of claims 29, 30, 33, 34, 37 and 38 under 35 U.S.C.112, first paragraph, new matter, is withdrawn in view of applicants' amendment to the claim, applicants'

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cancellation of the claim, and applicants' response at pages 6-7 of the amendment filed January 3, 2006.

Withdrawn Claim Rejections-Obviousness Type Double Patenting

6. The previous rejection of claims 18, 19, 29, 30, 33, 34 and 37 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 10-12 and 18 of co-pending application 10/270,010, is withdrawn in view of applicants' submission of a terminal disclaimer, applicants' cancellation of the claim, and applicants' response at page 7 of the amendment filed January 3, 2006.

7. The previous rejection of claims 18 and 19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5 of co-pending application 10/336,312, is withdrawn in view of applicants' submission of a terminal disclaimer, and applicants' response at pages 7-8 of the amendment filed January 3, 2006.

Claim Objections

8. Claims 18 and 19 are objected to because of the recitation of the phrase "wherein said isolated peptide is devoid of a disulfide bond". Since the isolated peptide consists of the sequence of SEQ ID NO:23, and the sequence does not have any cysteine residue, thus the phrase does not add any limitation to the claim. Deletion of the phrase is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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9. Claims 20 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of vectoring a chemical molecule to a target cell *in vitro* using the conjugate of a chemical molecule with the sequence of SEQ ID NO:23, wherein the chemical molecule is doxorubicin or an antitumor or antibacterial agent, does not reasonably provide enablement for a method of vectoring a chemical molecule to a target *in vitro* using a conjugate of the chemical molecule and a linear peptide having (read as comprising) or consisting of SEQ ID NO:23, wherein the target is a particular cell, a particular cell compartment, or a particular organ. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 20 and 24 are directed to a method of vectoring a chemical molecule to a target *in vitro* using a conjugate of the chemical molecule and a linear peptide comprising or consisting of SEQ ID NO:23, wherein the target is a particular cell, a particular cell compartment, or a particular organ. The specification, however, only discloses cursory conclusions (page 8, line 19-page 13, line 7) without data supporting the findings, which state that the peptide derived from an antibiotic peptide having the formula (I) or (II), and a compound of formula (IV) containing the peptide, an active substance and a signal agent, can be used to vector one or more active substances for therapeutic and for diagnostic applications. There are no indicia that the present application enables the full scope in view of the method of vectoring a chemical molecule using the linear peptide comprising SEQ ID NO:23 as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is

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required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the presence or absence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the linear peptides comprising the sequence of SEQ ID NO:23, and the chemical molecules for vectoring, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification only demonstrates specific analogs of protegrin and tachyplesin (e.g., SEQ ID NO:23 and other linear peptides in Tables I and II); the conjugates of the peptide with doxorubicin or biotin; and the internalization abilities of these peptides in different cell lines (Tables III and IV; Examples 1-4), where these in vitro results were the basis for vectoring an active substance in an organism. However, there are no working examples indicating all peptides comprising the sequence of SEQ ID NO:23 can vector different chemical molecules into a particular target cell, cell compartment, or organ in vitro.

(3). The state of the prior art and relative skill of those in the art:

The related art has shown certain analogs of protegrin and tachyplesin (e.g., pages 20-22 in Lehrer *et al.* WO 96/37508), which do not have cysteines and have decreased antimicrobial activity as compared to peptides having disulfide bonds. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to

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provide specific guidance on the vectoring effect of a peptide comprising the sequence of SEQ ID NO:23; identities of various chemical molecules; and the effect of the conjugate in vectoring a chemical molecule in vitro to be considered enabling for all variants.

(4). Predictability or unpredictability of the art:

The specification indicates certain linear peptides in Table III (protegrin peptides including SEQ ID NO:23) and Table IV (tachyplesin peptides) have internalization ability toward certain cell lines (in vitro), and it appears an increase in amphipathicity have positive effect in the protegrin family, however, the specification does not provide sufficient teachings regarding internalization ability of peptides comprising SEQ ID NO:23 in the conjugate, thus it is not readily apparent that one would have been able to predict the degree of internalization ability of a peptide comprising SEQ ID NO:23 and the vectoring effect of the conjugate containing various chemical molecules and peptide comprising SEQ ID NO:23.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claimed invention is directed to a method of vectoring a chemical molecule to a particular target cell, cell compartment, or organ using a conjugate of chemical molecules and a linear peptide comprising SEQ ID NO:23. The specification only discloses specific analogs of protegrin and tachyplesin (e.g., SEQ ID NO:23 and other linear peptides in Tables I and II); the conjugates of the peptide with doxorubicin or biotin; and the internalization abilities of these peptides in different cell lines (Tables III and IV; Examples 1-4). However, the specification has not demonstrated the vectoring effects of various linear peptides comprising the sequence of SEQ ID NO:23 in targeting various chemical molecules to a particular target cell, cell

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compartment, or organ. There are no working examples indicating the claimed variants and associated methods except for the conjugate of biotin-peptide or doxorubicin-peptide in vitro. Since the specification does not provide sufficient teachings on the vectoring effect of various peptide comprising SEQ ID NO:23 in targeting various chemical molecules to a particular target cell, cell compartment, or organ, it is necessary to carry out undue experimentation to assess the effects of the linear peptides comprising SEQ ID NO:23 in vectoring various chemical molecules to target cells, the experimentation is undue because further research is required to identify the active peptide comprising SEQ ID NO:23.

(6). Nature of the Invention

The scope of the claims encompass many variants in the claimed method, but the specification does not provide sufficient teachings on the effect of the linear peptide comprising SEQ ID NO:23 in vectoring various chemical molecules to target cells, cell compartments or organs. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods associated with variants, the teachings in the specification are limited, the effect of the conjugate is unpredictable, therefore, it is necessary to carry out undue experimentation to identify the active peptides and to assess the effects of the peptides in vectoring a chemical molecule to a particular target cell, cell compartment or organ.

Response to Arguments

Applicants indicate the claims have been amended to recite a method of vectoring the chemical molecule to a target in vitro using the conjugate of the chemical molecule with the

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sequence of SEQ ID NO:23. The amended claims when read in light of the specification, comply with the requirement under 35 U.S.C. 112, first paragraph (page 7 of the response).

Applicants' response has been fully considered, however, the argument is not found persuasive regarding the make/use of a linear peptide having (read as comprising) SEQ ID NO:23 in vectoring various chemical molecules because the specification only shows internalization abilities of specific peptides of protegrin and tachyplesin (e.g., SEQ ID NO:23 or other linear peptides in Tables III and IV) in different cell lines (Example 3, *in vitro* experimentation) and the internalization of the conjugate of SM 1738 (SEQ ID NO:15) and doxorubicin (Example 4), it has not demonstrated the vectoring effects of various peptides comprising SEQ ID NO:23 in vectoring various chemical molecules to a particular cell compartment, cell or organ, as encompassed by the claims (see above). Since the specification does not provide sufficient teachings on the linear peptides comprising SEQ ID NO:23 and their effects in vectoring various chemical molecules, it requires undue experimentation to identify the active linear peptides comprising SEQ ID NO:23 in vectoring chemical molecules to the target. Thus, the specification is only enabling for a linear peptide consisting of SEQ ID NO:23, and its effect in vectoring a chemical molecule of biotin, doxorubicin, an antitumor or antibacterial agent to a target cell *in vitro*.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claims 20, 24 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 20 and 24 are indefinite because the claim recites a method for vectoring a chemical molecule to a target *in vitro*, it is not clear how the target can be a particular organ for *in vitro* method. Claims 20 and 24 are also indefinite as to how to couple the conjugate of the chemical molecule to the linear peptide in step (a) since the conjugate is obtained by coupling of a chemical molecule and the linear peptide.

12. Claim 29 is indefinite, it is not clear how the linear peptide (A) is coupled to a chemical molecule (Z) in formula (IV), e.g., is it covalent, ionic or hydrophobic bond.

Claim Objection

13. Claim 30 is objected to because the claim depends from a rejected claim, claim 29.

Conclusion

14. Claims 20, 24 and 29 are rejected; claims 18, 19 and 30 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



CHIH-MIN KAM
PATENT EXAMINER

CMK

March 10, 2006